WHAT WE CLAIM IS:

1. A method for the long term culture of hepatocyte cells comprising the steps:

commuting hepatocyte tissue in cold DMEM and incubating for up to 24 hours at 4°C;

twice digesting with liberase® at a concentration of 0.2mg/ml in the presence of lignocaine;

separating the digested hepatocyte cells; and

culturing in media comprising allogeneic serum,

wherein said hepatocytes are capable of secreting one or more liver secretory factors for extended periods in culture.

2. A method as claimed in claim 1, wherein the hepatocytes are neonatal hepatocytes.

3. A method for the long term culture of at least one non-hepatocyte cell type capable of secreting one or more liver secretory factors, said method comprising the steps:

commuting non-hepatocyte tissue in cold DMEM and incubating for up to 24 hours at 4°C;

twice digesting with liberase® (0.2 mg/ml) for up to 10 minutes in the presence of lignocaine;

separating the digested non-hepatocyte cells; and

culturing in media comprising allogeneic serum,

wherein said at least one non-hepatocyte cell type is selected from the group consisting of gall bladder epithelial cells, gall bladder endothelial cells, bile duct epithelial cells, bile duct endothelial cells, hepatic vessel epithelial cells, hepatic vessel endothelial cells, sinusoid cells and non-parenchymal liver cells.

4. A method as claimed in claim 3, further including the step of co-culturing the non-hepatocyte cells with hepatocytes.

5. A method as claimed in claim 4, wherein the non-hepatocyte cells and/or hepatocyte cells are neonatal cells.

6. A method as claimed in any preceding claim, wherein the at least one

non-hepatocyte cell type and/or hepatocytes are pig or human cells.

7. A method as claimed in any one of claims 1-6, wherein the one or more liver secretory factors are selected from the group comprising albumin, blood clotting factors such as factor VIII or factor IX, growth and/or differentiation factors such as growth hormone and analogues thereof, insulin-like growth factor and analogues thereof, hepatocyte growth factor and analogue thereof, fibroblast growth factor and analogues thereof; or hormones such as corticosteroids.

8. A method of producing one or more liver secretory factors in vitro from at least one non-hepatocyte cell type selected from the group consisting of gall bladder epithelial cells, gall bladder endothelial cells, bile duct epithelial cells, bile duct endothelial cells, hepatic vessel epithelial cells, hepatic vessel endothelial cells, sinusoid cells and non-parenchymal liver cells, said method comprising the steps of:

isolating said at least one non-hepatocyte cell type;

culturing said at least one non-hepatocyte cell type in media supplemented with allogeneic serum for a time sufficient to allow secretion of said one or more liver secretory factors into the media;

harvesting said media; and

optionally isolating or purifying said liver secretory factors.

9. A method as claimed in claim 8, wherein the at least one non-hepatocyte cell type is co-cultured with hepatocyte cells.

10. A method as claimed in claim 8 or claim 9, wherein said at least one non-hepatocyte cell type and/or hepatocyte is isolated from neonatal tissue.

11. A method as claimed in any one of claims 8-10, wherein said at least one non-hepatocyte cell and/or hepatocyte is a pig or human cell.

12. An implantable composition comprising at least one non-hepatocyte cell type capable upon implantation into a recipient of secreting one or more liver secretory factors or of providing one or more liver metabolic and/or physiologic functions to said recipient, wherein said one or more non-hepatocyte cell type is selected from the group consisting of gall bladder epithelial cells, gall bladder

endothelial cells, bile duct epithelial cells, bile duct endothelial cells, hepatic vessel epithelial cells, hepatic vessel endothelial cells, sinusoid cells and non-parenchymal liver cells.

13. A composition as claimed in claim 12 further comprising hepatocyte cells.

14. A composition as claimed in claim 12 or 13 wherein the at least one non-hepatocyte cell type and/or hepatocyte cells are neonatal cells.

15. A composition as claimed in any one of claims 12-14, wherein the at least one non-hepatocyte cell type and/or hepatocyte cells are pig or human cells.

16. A method of producing one or more liver secretory factors in vivo, comprising the step of implanting a composition as claimed in any one of claims 12-15 into a patient in need thereof.

17. A method as claimed in claim 16 wherein said composition provides liver secretory factors or provides liver metabolic or physiologic functions over an extended period post implantation.

18. An implantable composition comprising one or more aggregates of at least one non-hepatocyte cell type capable upon implantation into a recipient, of producing and/or secreting one or more liver secretory factors, wherein said at least one non-hepatocyte cell type is selected from the group consisting of gall bladder epithelial cells, gall bladder endothelial cells, bile duct epithelial cells, bile duct endothelial cells, hepatic vessel epithelial cells, hepatic vessel endothelial cells, sinusoid cells and non-parenchymal liver cells .

19. An implantable composition as claimed in claim 15 wherein the aggregates further comprise hepatocyte cells.

20. An implantable composition as claimed in claim 18 or 19 wherein the at least one non-hepatocyte cell type and/or hepatocyte cells are pig or human cells.

21. A method as claimed in claim 9 or a composition as claimed in claim 13 or 19, wherein the hepatocytes are isolated from immortalised cells in commercially available cell cultures.

22. A composition as claimed in claim 12 or 18, wherein the at least one non-hepatocyte cell type comprises gall bladder endothelial and/or epithelial cells.

23. A composition as claimed in claim 22, comprising gall bladder epithelial cells.

24. A composition as claimed in claim 23 further comprising hepatocytes in a ratio of between 0.5:2 and 2:0.5 gall bladder epithelial cells: hepatocytes.

25. A composition as claimed in claim 24, wherein the ratio of gall bladder epithelial cells: hepatocytes is 1:1.

26. A composition as claimed in claim 12 or 18, wherein the one or more liver secretory factors is a blood clotting factor.

27. A composition as claimed in claim 26, wherein the blood clotting factor is Factor VIII and/or Factor IX.

28. A composition as claimed in claim 27, wherein when the blood clotting factor is Factor VIII, von Willebrand factor is co-secreted.

29. A composition as claimed in claim 12 or 18, wherein the one or more liver secretory factors is a growth and/or differentiation factor.

30. A composition as claimed in claim 29, wherein the growth and/or differentiation factor is selected from growth hormone and analogues thereof, insulin like growth factor and analogues thereof, hepatocyte growth factor and analogues thereof, or fibroblast growth factor and analogues thereof.

31. A composition as claimed in claim 12 or 18, wherein the one or more liver secretory factors is an enzyme.

32. A composition as claimed in claim 12 or 18, wherein said non-hepatocyte cell types are derived from the same species as the recipient.

33. A method of treating a patient suffering from or predisposed to a disease or condition associated with a deficiency in or absence of a liver secreted factor comprising the implantation of an effective amount of one or more implantable compositions as claimed in any one of claims 12-32, to a patient in need thereof.

34. A method as claimed in claim 33, wherein said disease or condition is chronic liver insufficiency, liver failure, liver disease, or alcoholic liver disease.

35. A method as claimed in claim 34, wherein said insufficiency, failure or disease is caused by infection with hepatitis A or B virus.

36. A method of treating a patient suffering from or predisposed to a blood clotting disease or condition comprising the implantation of an effective amount of one or more implantable compositions of the invention to a patient in need thereof.

37. A method of treating a patient suffering from or predisposed to hemophilia and/or a blood-clotting disease or disorder comprising the implantation of an effective amount of one or more implantable compositions as claimed in any one of claims 12-32 to a patient in need thereof.

38. A method as claimed in claim 37, wherein said hemophilia is hemophilia A.

39. A method as claimed in any one of claims 33 to 38, wherein the implantable composition of any one of claims 12 to 32 comprises cells encapsulated in a suitable biocompatible material such as alginate;

cells confined in a suitable device, such as a vascularized tube or Theracyte™ device;

cells encapsulated in matrix preparations such as gelatin, collagen, and/or natural carbohydrate polymers; and/or

cells confined in a plasma thrombin clot including allogeneic plasma clots produced with allogeneic thrombin.

40. A method of administering a blood clotting factor to a patient in need thereof, wherein said blood clotting factor is complexed and/or associated with one or more factors capable of enhancing the activity, stability, bioavailability, and/or efficacy of said blood clotting factor, wherein the method comprises the implantation of an effective amount of one or more implantable compositions as claimed in any one of claims 12 to 32 to said patient.

41. A method as claimed in claim 40, wherein the blood clotting factor is Factor VIII, and said one or more factors capable of enhancing the activity, stability, bioavailability, and/or efficacy of said blood clotting factor is von Willebrand factor.

42. A method of treating a patient suffering from or predisposed to a disease or condition associated with a deficiency in a metabolic and/or physiologic function

of the liver, said method comprising the implantation of an effective amount of one or more implantable compositions of any one of claims 12 to 32 to the patient.

43. A method as claimed in claim 42, wherein the disease or condition comprises chronic liver insufficiency, liver failure, liver disease, or alcoholic liver disease.

44. A use of at least one non-hepatocyte cell type selected from the group consisting of gall bladder epithelial cells, gall bladder endothelial cells, bile duct epithelial cells, bile duct endothelial cells, hepatic vessel epithelial cells, hepatic vessel endothelial cells, sinusoid cells and non-parenchymal liver cells in the manufacture of a medicament for treating a patient suffering from or predisposed to a disease or condition associated with a deficiency in or absence of a liver secreted factor or suffering from or predisposed to a disease or condition associated with a deficiency in a metabolic and/or physiologic function of the liver.

45. A use as claimed in claim 44, wherein said disease or condition is chronic liver insufficiency, liver failure, liver disease, or alcoholic liver disease.

46. A use of at least one non-hepatocyte cell type selected from the group consisting of gall bladder epithelial cells, gall bladder endothelial cells, bile duct epithelial cells, bile duct endothelial cells, hepatic vessel epithelial cells, hepatic vessel endothelial cells, sinusoid cells and non-parenchymal liver cells in the manufacture of a medicament for treating a patient suffering from or predisposed to a blood clotting disease or condition, such as hemophilia, and in particular, hemophilia A.

47. A use as claimed in any one of claims 44-46 which said medicament further comprises hepatocyte cells.

48. A use as claimed in claim 47, wherein said medicament comprises gall bladder epithelial cells and hepatocytes in a ratio of 0.5:2 to 2:05, preferably in a ratio of 1:1.

49. A use as claimed in any one of claims 45-48, wherein the medicament comprises cells encapsulated in a suitable biocompatible material, such as alginate;

cells confined in a suitable device, such as a vascularized tube or Theracyte™ device;

cells encapsulated in matrix preparations such as gelatin, collagen, and/or natural carbohydrate polymers; and/or

cells confined in a plasma thrombin clot including allogeneic plasma clots produced with allogeneic thrombin.

50. A device for implantation into a recipient suffering from or predisposed to a disease associated with a deficiency in or absence of a secreted liver factor, the device comprising one or more implantable compositions as claimed in any one of claims 12-32.

51. A device as claimed in claim 50 comprising a capsule comprising a suitable biocompatible material such as alginate;

a vascularized tube or chamber, more preferably a TheraCyte™ device available from TheraCyte, Inc., CA;

a matrix preparation comprising gelatin, collagen, and/or natural carbohydrate polymers; or

a plasma thrombin clot including an allogeneic plasma clot produced with allogeneic thrombin.